REMARKS

Claims 1-40 are pending in the instant application. Claims 1-11, 16-21 and 23-40 have been cancelled without prejudice or disclaimer, claims 12, 13, 22, and 41 have been amended and claims 42-45 have been added. Page 1 of the specification has been amended to correct the statement of government support. Accordingly, claims 12-15, 22 and 41-45 will be pending in the application upon entry of the amendments presented herein.

Support for the claim amendments and additions can be found throughout the specification and claims as originally filed. In particular, support for the amendment of claims 12 and 22 can be found at least, for example, in original claims 16-21 and in the application on page 26, lines 10-14; support for the addition of claims 42-43 can be found at least, for example, in original claims 13-15; support for the amendment of claims 13 and 41, which now recites "epithelial cell, endothelial cell, mesothelial cell, dendritic cell, spenocyte, macrophage" is found, for example, at page 8, lines 17-21, and support for the addition of claims 44 and 45 can be found at least, for example, in the application in Example 1 (page 36) and Example 5 (page 42). No new matter has been added.

Amendment and cancellation of the claims are not to be construed as acquiescence to any rejections and/or objections set forth in the Office Action and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the subject matter of the claims as originally filed in this application or one or more subsequent patent applications.

Claim Rejections – 35 USC § 102

Claims 12-22 are rejected under 35 U.S.C. §102(a) as being anticipated by US Patent No. 6,316,410 (hereinafter referred to as "Barbier"). Specifically, the Office Action indicates that Barbier "...does not explicitly teach[es] that administering of said PTH would enhanced the growth of hematopoietic progenitor cells. However, the referenced method administered the same treatment, i.e. PTH or PTH analogue to the

same subject under the same treatment. Under the principles of inherency, if the prior art structure, is capable of performing the intended use, then it meets the claim."

Applicants respectfully disagree and traverse the rejection. However, without acquiescing in any way to the rejection and in order to expedite prosecution, Applicants have amended claim 12 to specify that the subject is a bone marrow donor who has donated bone marrow, is a bone marrow donor who has yet to donate bone marrow, is a bone marrow transplant recipient, has hematopoietic progenitor cells under environmental stress, or has anemia. Applicants have amended claim 22 to specify that the subject is a bone marrow donor who has donated bone marrow or is a bone marrow donor who has yet to donate bone marrow.

Barbier describes the treatment of osteoporosis by administering analogues of human parathyroid hormone. Barbier does not teach or suggest the administration of an agent that activates the PTH/PTHrP receptor in cells of the subject expressing the PTH/PTHrP receptor to a subject who is a bone marrow donor who has donated bone marrow, is a bone marrow donor who has yet to donate bone marrow, is a bone marrow transplant recipient, has hematopoietic progenitor cells under environmental stress, or has anemia. Thus, the method of claims 12 and 22 presented herein does not administer the same treatment to the same subject in need of such treatment. The subject recited in the claims and the subject disclosed in Barbier are clearly different. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 12-22 were rejected under 35 U.S.C. §102(b) as being anticipated by US Patent No. 5,747,456 (hereinafter referred to as "Chorev"). Specifically, the Office Action sets forth the allegation that Chorev "...does not explicitly teach[es] that administering of said PTH would enhanced the growth of hematopoietic progenitor cells. However, the referenced method administered the same treatment, i.e., PTH or PTH analogue to the same subject in need of such treatment. Under the principles of inherency, if the prior art structure, is capable of performing the intended use, then it meets the claim." Applicants respectfully disagree and traverse the rejection.

As mentioned above, Applicants have amended claims 12 to specify that the subject is a bone marrow donor who has donated bone marrow, is a bone marrow donor who has yet to donate bone marrow, is a bone marrow transplant recipient, has hematopoietic progenitor cells under environmental stress, or has anemia; claim 22 has been amended to specify that the subject is a bone marrow donor who has donated bone marrow or is a bone marrow donor who has yet to donate bone marrow. Chorev describes the promotion of bone formation in a patient suffering from osteoporosis by administering continuously parathyroid hormone or its agonist. Chorev neither teaches nor suggests the administration of an agent that activates the PTH/PTHrP receptor in cells of the subject expressing the PTH/PTHrP receptor to a subject who is a bone marrow donor who has donated bone marrow, is a bone marrow donor who has yet to donate bone marrow, is a bone marrow transplant recipient, has hematopoietic progenitor cells under environmental stress, or has anemia.

Thus, the method of claims 12 and 22 presented herein does not administer the same treatment to the same subject in need of such treatment. The subject recited in the claims and the subject disclosed in Cherov are clearly different. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 12-22 are rejected under 35 U.S.C. §102(e) as being anticipated by US Patent No. 6,342,477 (hereinafter referred to as "Tamura"). Specifically, Office Action alleges that Tamura "...does not explicitly teach[es] that administering of said PTH would enhanced the growth of hematopoietic progenitor cells. However, the referenced method administered the same treatment, i.e., PTH or PTH analogue to the same subject in need of such treatment. Under the principles of inherency, if the prior art structure, is capable of performing the intended use, then it meets the claim." Applicants respectfully disagree and traverse the rejection.

M.P.E.P. §2112 (IV) directs that the Examiner must provide rationale or evidence tending to show inherency:

> "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)...*In re Oelrich*, 666 F.2d 578, 581-82,

> 212 USPQ 323, 326 (CCPA 1981). 'To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill'...*In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)...In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic **necessarily** flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). [Emphasis added.]

The current law of the Doctrine of Inherency indicates that the claimed property or therapeutic effect must be the **necessary** consequence of the prior art disclosure. In other words, every time one conducts the prior art process, the claimed property or therapeutic effect **must** occur. If one conducts the prior art method and does not get the claimed property or therapeutic effect, then the claimed process is not inherent in the prior art.

The methods disclosed in Tamura involve administration of PTH or a PTH derivative to a thrombocytopenic subject over at most a 13-day period (see Examples 1-4). In this regard, Applicants invite the Examiner's attention to Example 5 of the application, which compares the hematopoietic stem cell population (for an increase) over a two-week treatment with PTH vs. a 4-week treatment of PTH. Notably, the two-week PTH treatment, akin to the treatment disclosed in Tamura "...did not result in any significant increase in the hematopoietic stem cell population, [whereas] treatment of mice for four weeks with PTH resulted in a significant increase in the hematopoietic stem cells over mock injected mice... These data are most consistent with [hematopoietic stem cell] HSC expansion by enhanced self-renewal, a phenomenon known to result from Notch activation..."

At most, the methods of Tamura are alleged to increase platelet count in a thrombocytopenic subject. In other words, practicing Tamura's methods of administration of PTH or a PTH derivative over a 13-day (less than 2-week) period

would not result in an enhancement of the growth or maintenance of **hematopoietic progenitor cells** in the subject as is achieved in accordance with the claimed methods.

Not only did the instantly claimed property (enhancement of the growth or maintenance of hematopoietic progenitor cells in the subject) **not necessarily** occur when the prior art (Tamura) process was conducted, but in fact, the effects demonstrated by Tamura are inconsistent with an effect on hematopoietic progenitor cells. Tamura observes increases in platelet count beginning at day 2 after PTH administration (Figure 2). This increase in platelet number at day two cannot result from an increase in hematopoietic progenitor cell number because Applicants show that the number of hematopoietic progenitor cells will not increase until **two weeks after administration of PTH**. Clearly, a treatment duration of 13 days would not be sufficient to bring about an enhancement of the growth or maintenance of hematopoietic progenitor cells.

Moreover, Tamura's results are contrary to what would be expected if platelet numbers were increased as a result of an increase in hematopoietic progenitor cell number. If platelet numbers changed due to an increase in hematopoietic progenitor cell number, then platelet numbers should increase steadily as hematopoietic progenitor cell numbers increase. Applicants show that hematopoietic progenitor cell numbers increase significantly following four weeks of PTH treatment. However, Tamura fails to observe a similar increase in platelet number. In fact, at Figure 4, Tamura shows that platelet numbers peak at day six in response to PTH treatment and then platelet numbers drop, reaching their original level by day 13. This observation is inconsistent with an effect on hematopoietic progenitor cells. The rapid, transient rise in platelet counts observed by Tamara is most consistent with a change in the location of existing platelets or fragmentation of the megakaryocytes from which platelets emerge. In sum, the PTH administration described by Tamura was not of sufficient duration to elicit an increase in hematopoietic progenitor cell number, and is inconsistent with the steady growth in platelet number that would be expected if platelet number increased as hematopoietic progenitor cell number increased.

Indeed, even if one of ordinary skill in the art were intent on increasing platelet count, she would not be motivated by the teachings of Tamura to conduct a longer treatment period. In this regard, Applicants invite the Examiner's attention to Tamura, column 6, lines 26-32:

> "Three rabbits were daily administered with 200 μg/kg of PTH and platelets were counted on day 0, 2, 6, 9 and 13 of the administration period. The results are shown in FIG. 4. Starting on day 2 of the administration, the platelet count increased until day 6, exhibiting two to four times as great as the initial value. **The platelet count substantially returned to the initial level on day 13**." [Emphasis added.]

Tamura **teaches** one of ordinary skill in the art **away** from treating for more than 13 days, much less four weeks as in Example 5. Accordingly, one of ordinary skill in the art would not expect any further increase in platelets by treating for periods greater than 13 days.

Thus, Applicants submit that the claimed process is **not** inherent in Tamura, and Tamura cannot be said to anticipate the claimed invention. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of all rejections and allowance of the application with claims 12-15, 22 and 41-45 presented herein. If a telephone conference with Applicants' attorney would be useful in expediting prosecution of the application, Applicants invite the Examiner to call the undersigned at the telephone number indicated below.

Dated: February 19, 2008

Respectfully submitted,

By_____

Melissa Hunter-Ensor
Registration No.: 55,289
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5580
Attorneys/Agents For Applicants